THE FORENSIC PANEL
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James P. Loonam, Esq.
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250 Vesey Street
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Re: Robert T. Brockman

October 29, 2021

Dear Mr. Loonam,

At your request, earlier this year I reviewed the available diagnostic imaging studies of Robert Brockman, an 80-year-old defendant who has been worked up for cognitive problems since 2018.

Mr. Brockman is charged in a complex indictment with details and history that require him to be actively engaged in informing his attorneys with reliable and valid information, to be making decisions, and to be guiding the attorneys through records and evidence. His capacity to inform his attorneys and to engage the mental and physical rigors of trial is in question, and a court hearing is anticipated.

I consulted on this matter with The Forensic Panel, in collaboration with primary examiners addressing other areas of expertise. These include Marc Agronin, M.D., a geriatric psychiatrist, Thomas Guilmette, Ph.D., a neuropsychologist, and Thomas Wisniewski, M.D., a neurologist. We each submitted reports to the court on August 6, 2021.

Since my report was filed, a number of additional neuroimaging studies have been conducted. You have asked me to review this additional data and other new pertinent information and write a supplemental report. The findings in this report do not replace my findings in the August 6 report. The conclusions addressed here are meant to complement my earlier findings.

RECENTLY REVIEWED SOURCES OF INFORMATION

1) FDG-PET scan, August 24, 2021
2) EEG report, September 2, 2021
3) Dr. Darby's Neuroreader report for 2018 MRI, August 20, 2021
4) Reports of Maria Ponisio, M.D., September 1, 2 and 5, 2021
5) Houston Methodist Hospitalization records, September 15-18, 2021
6) CT scan images, September 16, 2021
7) Marc Agronin, M.D. report, October 29, 2021
8) Thomas Guilmette, Ph.D report, October 29, 2021

9) Thomas Wisniewski, M.D report, October 29, 2021

FORENSIC NEURORADIOLOGY ASSESSMENT

What does the recent neuroimaging in this case inform about the nature and severity of Mr. Brockman's diagnosis?

Mr. Brockman has known Parkinson's disease, which is associated with development of overt dementia (i.e., Parkinson's disease dementia; PDD) that occurs among Parkinson's disease patients with a prevalence of approximately 70%.[1] Mr. Brockman demonstrates significant cognitive impairment across numerous neuropsychological instruments, which has progressed over time.

PET Scans

The most recent FDG-PET scan from August 24, 2021 demonstrates persistent diminished metabolic activity compared to FDG-PET scan dated March 12, 2021, especially in areas important to cognitive function and in a pattern compatible with Alzheimer's disease, specifically in temporal and parietal lobes.

Overall, the anatomical pattern of diminished metabolic activity is similar between the two recent FDG-PET scans, though may have progressed slightly to involve more of the brain.[2]

The anatomical pattern of Mr. Brockman's brain hypometabolism (i.e., diminished brain energy utilization) abnormality on the August 24, 2021 FDG-PET imaging is consistent with and suggestive of Alzheimer's disease. This finding of hypometabolism alone is, however, non-specific for an Alzheimer's diagnosis. The pathophysiology of Alzheimer's disease results in abnormal accumulation of proteins in the brain, such as beta-amyloid (Aβ), which cannot be characterized by FDG-PET. The use of beta-amyloid PET imaging (e.g., Amyvid PET), therefore, is used clinically to look for this more specific evidence of abnormal beta-amyloid accumulation that is one of the hallmarks of Alzheimer's disease.

As noted in my August 6 report, Mr. Brockman's July 28, 2021 beta-amyloid PET scan was positive for abnormally increased uptake in the cortical gray matter indicating moderate to frequent beta-amyloid plaques, as can be seen in patients with Alzheimer's disease. It should be noted that a positive beta-amyloid PET scan does not confirm the diagnosis of Alzheimer's disease. Rather, the presence of beta-amyloid plaques in a patient with cognitive impairments increases the probability that this impairment is due to Alzheimer's

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[1] Painous, Celia, and Maria J. Marti**. Cognitive impairment in Parkinson's disease: what we know so far.** *Journal of Parkinsonism & Restless Legs Syndrome* 10 (2020): 7.

[2] **Fluorodeoxyglucose Positron Emission Tomography in Autopsy-Confirmed Dementia**. *Ann Neurol.* 2021 Feb;89(2):389-401.

disease, and in this way, beta-amyloid PET scans serve as an adjunct to other diagnostic evaluations that together are used in the assessment of Alzheimer's disease. Specifically, beta-amyloid PET data are combined with converging evidence from other brain imaging (e.g., MRI assessment of volume and FDG-PET assessment of metabolism), as well as performance on assessments of cognitive function to better resolve, from a clinical standpoint, the possible diagnosis of Alzheimer's disease.

The importance of cumulative imaging data is illustrated by one recent study that combined qualitative results from beta-amyloid PET imaging and FDG-PET scans in diagnosing Alzheimer's disease. In this study, sensitivity and specificity for diagnosis of Alzheimer's disease approached 100% compared to gold-standard brain tissue pathology results when beta-amyloid PET was positive for cortical beta-amyloid and FDG-PET demonstrated the typical AD hypometabolism pattern. This AD pattern is the predominant hypometabolism of posterior cingulate/precuneus and/or lateral temporoparietal areas of the cortex.

Mr. Brockman's beta-amyloid PET scan and FDG-PET scan meet the criteria of cortical beta-amyloid positivity and Alzheimer's disease-like anatomical pattern of hypometabolism that are highly suggestive of Alzheimer's disease. As such, these imaging findings support the conclusion that he likely has Alzheimer's disease in addition to Parkinson's disease, and are consistent with demonstrated dementia on neuropsychological testing and functional decline observed by those who interact with him daily.

It should be noted that the beta-amyloid PET tracer used to diagnose Mr. Brockman was Amyvid, whereas the beta-amyloid PET tracer used in the research study cited above was Pittsburgh Compound-B (PiB). PiB is labeled with ^{11}C and confided primarily to research studies due to the relatively short tracer half-life (20 minutes). In contrast, Amyvid is labeled with ^{18}F that has a longer tracer half-life (110 minutes), which is better suited and FDA-approved for diagnostic imaging in clinical practice when Alzheimer's disease is suspected.

Both PET tracers have been shown to be highly correlated with respect to characterizing burden of cortical beta-amyloid, and both are highly correlated with clinical and cognitive measurements.[3] As such, the FDG-PET + PiB research findings would translate clinically to Mr. Brockman's imaging evaluation that used FDG-PET + Amyvid.

Taken together, the newest imaging findings add to available evidence that Mr. Brockman is experiencing a progressive neurodegenerative process and support Mr. Brockman's cognitive testing results. FDG-PET hypometabolism in frontal lobes, for example, supports findings of cognitive dysfunction in domains subserved by this area of the brain,

[3] Su Y, Flores S, Wang G, et al. **Comparison of Pittsburgh compound B and florbetapir in cross-sectional and longitudinal studies**. *Alzheimers Dement (Amst)* 2019;11:180-90.

such as decision-making, problem solving, impulsivity, sustained attention and other functions that may add to the morbidity of memory and cognitive decline.

MRI and CT Scans

Mr. Brockman underwent MRI scans of the brain on November 2, 2018, and June 6 and July 30, 2021. The data demonstrates brain volumetric loss from the 2018 MRI to the 2021 MRI scans. Structural brain volume loss or atrophy as an isolated finding on MRI is a non-specific abnormality, but when associated with cognitive functional deterioration raises concern for an underlying neurodegenerative process. The most recent brain MRI (from July 30, 2021) and head CT (September 16, 2021) demonstrate persistent diffuse cerebral volume loss and chronic microvascular ischemic disease of the white matter, including volume loss/atrophy in areas important for cognitive function. The magnitude of overt visually obvious volume loss on MRI relative to Mr. Brockman's MRI of 2018 is beyond anything that would be reversible, and this is true for both MRI scans (June 6 and July 30) performed in 2021.

Quantitative volumetric analyses have also been performed using brain MRI data from the November 2, 2018 and July 30, 2021 scans. Brain volumetric analysis results described in the Neuroreader Report based upon the July 30, 2021 scan support the qualitative observation of volume loss, including in areas important for cognitive function. The Neuroreader Report associated with the July 30, 2021 scan demonstrates volume loss in more brain areas compared to the previous November 2, 2018 scan/Neuroreader Report.

However, conclusions on interval volume loss using Neuroreader are confounded by known measurement error (such as inter-scanner variability) associated with quantitative brain MRI volumetric analyses.[3] Therefore, while the Neuroreader data is consistent with other data supporting degenerative brain disease, these are not data that contribute to the certainty of a dementia diagnosis in any manner comparable to FDG-PET, beta-amyloid PET, neuropsychological testing using standardized protocols, and clinical history of functional decline based on inadequate ability to meet day-to-day cognitive needs.

Reports of Dr. Maria Ponisio on Neuroimaging

The analyses provided by Dr. Ponisio do not synthesize the cumulative imaging data -- specifically the beta-amyloid PET scan, multiple FDG-PET scans, multiple MRI scans -- and cognitive data. Such a synthesis would be expected in a standard neuroradiology evaluation.

Summary

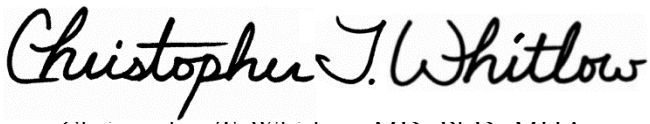
Primary differential consideration and underlying etiology for Mr. Brockman's neurodegenerative disease with dementia include Parkinson's disease, with which Mr.

Brockman is diagnosed, as well as comorbid Alzheimer's disease. Newly published data in the peer-reviewed literature on the combined use of beta-amyloid PET and FDG-PET in diagnosing Alzheimer's disease adds substantially to informing the most likely diagnosis based on Mr. Brockman's neuroimaging and cognitive testing results. His amyloid positivity and pattern of hypometabolism on recent PET scans in particular points to Alzheimer's disease as at least one cause (along with Parkinson's Disease Dementia) of his ongoing neurodegenerative process.

In clinical practice, the prognosis for Mr. Brockman's Parkinson's Disease Dementia and Alzheimer's disease-like combination of cognitive decline, brain volume loss, hypometabolism and brain beta-amyloid proteinopathy would be poor. In the case of Mr. Brockman, the expectation/prognosis would be that of continued cognitive decline, which would be irreversible and have a high probability of increasing velocity over time, ultimately associated with a significant increase in mortality.

Thank you for the opportunity to review this matter.

Sincerely yours,



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